

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|----|------|-----|------|----------------------------------------|------------------------------------------|----------------------|----------|------------------|--------|
| 1 | BRS | L1 | 1750 | lactoferrin | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:26 | | | 0 |
| 2 | BRS | L2 | 0 | fragment adj 20-31 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:26 | | | 0 |
| 3 | BRS | L3 | 154 | 1 same (fragment or analog or homolog) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:34 | | | 0 |
| 4 | BRS | L4 | 0 | 3 same 20-31 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:28 | | | 0 |
| 5 | BRS | L5 | 6 | 3 same cycli\$3 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:29 | | | 0 |
| 6 | BRS | L6 | 1 | 3 same (acetyl\$4 or amidat\$3) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:33 | | | 0 |
| 7 | BRS | L7 | 5386 | medical adj product | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:34 | | | 0 |
| 8 | BRS | L8 | 0 | 3 same 7 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:35 | | | 0 |
| 9 | BRS | L9 | 5105 | food adj stuff | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:35 | | | 0 |
| 10 | BRS | L10 | 0 | 3 same 9 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:36 | | | 0 |
| 11 | BRS | L11 | 1089 | infant adj formula | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:35 | | | 0 |
| 12 | BRS | L12 | 1 | 3 same 11 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:39 | | | 0 |

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Error |
|----|------|-----|------------|------------------------------------------------------------------------------------------------------|------------------------------------|-------------------|----------|------------------|-------|
| 13 | BRS | L13 | 18025 1 | infection or inflammation or (urinary adj tract adj infection) or colitis or (candida adj infection) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:39 | | | 0 |
| 14 | BRS | L14 | 23 | 3 same 13 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:46 | | | 0 |
| 15 | BRS | L15 | 2 | 5304633.pn. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:46 | | | 0 |
| 16 | BRS | L19 | 0 | dolphin adj gunnar.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:57 | | | 0 |
| 17 | BRS | L16 | 2 | hanson adj lars.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:57 | | | 0 |
| 18 | BRS | L17 | 3 | baltzer adj lars.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:58 | | | 0 |
| 19 | BRS | L18 | 1 | mattsby-baltzer adj inger.in. | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/02/2 6 11:59 | | | 0 |

FILE 'HOME' ENTERED AT 12:10:39 ON 26 FEB 2003

=> file medline caplus biosis embase scisearch agricola
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FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 12:11:04 ON 26 FEB 2003

FILE 'CAPLUS' ENTERED AT 12:11:04 ON 26 FEB 2003
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FILE 'AGRICOLA' ENTERED AT 12:11:04 ON 26 FEB 2003

=> s lactoferrin
L1 20298 LACTOFERRIN

=> s (peptide or fragment or analog) (p) l1
L2 1889 (PEPTIDE OR FRAGMENT OR ANALOG) (P) L1

=> s l2 (p) 21-30
L3 0 L2 (P) 21-30

=> s l2 (p) cycli?
L4 20 L2 (P) CYCLI?

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L4
L5 9 DUPLICATE REMOVE L4 (11 DUPLICATES REMOVED)

=> d l5 1-9 ibib abs

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:234495 CAPLUS
TITLE: The structures and membrane interactions of
 lactoferricin B derived peptides
AUTHOR(S): Schibli, D. J.; Vogel, H. J.
CORPORATE SOURCE: Department of Biological Sciences, University of
 Calgary, Calgary, AB, Can.
SOURCE: Biochemistry and Cell Biology (2002), 80(1), 163

CODEN: BCBIEQ; ISSN: 0829-8211

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lactoferricin B (Lfcin B) is a 25-residue ***fragment*** of the 80 kDa iron-binding protein ***lactoferrin***, which is released upon pepsin digestion. The NMR soln. structure of Lfcin B was previously shown to form a twisted sheet in H₂O. This differs from the helix-sheet structure that the Lfcin B sequence adopts in the native ***lactoferrin*** protein. The 6-residue antimicrobial center of Lfcin B (LfcinB4-9; RRWQWR-NH₂) possesses similar antimicrobial activity to the intact ***peptide***. We have recently detd. the structure of LfcinB4-9, bound to sodium dodecyl sulfate (SDS) micelles by NMR spectroscopy. We are currently expanding our NMR studies of Lfcin B derived ***peptides*** to include an 11-residue ***fragment*** of Lfcin B (LfcinB4-11; RRWQWRMLLLG) as well as a disulfide ***cyclized*** variant of LfcinB4-11. All of these ***peptides*** were detd. to be flexible in aq. soln. but form stable amphipathic structures when bound to SDS micelles. Addnl. we have investigated the interactions Lfcin B, LfcinB4-9, and LfcinB4-11 with large unilamellar vesicles (LUVs) using fluorescence spectroscopy. The results are consistent with the Trp-residues being inserted in a hydrophobic environment. Evidence suggests that these ***peptides*** are found at the membrane-water interface of LUVs. Burial of the Trp-residues appears to be greater in vesicles that contain a phospholipid with an anionic head group. Addnl., differential scanning calorimetry (DSC) data demonstrate that both Lfcin B and LfcinB4-9 will raise the bilayer to hexagonal phase transition temp. of DiPoPE. This suggests that these ***peptides*** do not favor lipid structures with overall neg. curvature, but instead promote pos. curvature strain in membranes. These results suggest that Lfcin B derived antimicrobial ***peptides*** may induce membrane lysis as a consequence of partitioning into the membrane interface and forming a membrane-bound amphipathic structure.

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:234451 CAPLUS

TITLE: Structural features of lactoferricin

AUTHOR(S): Vogel, H.

CORPORATE SOURCE: Department of Biological Sciences, University of Calgary, Calgary, AB, T2N 1N4, Can.

SOURCE: Biochemistry and Cell Biology (2002), 80(1), 141

CODEN: BCBIEQ; ISSN: 0829-8211

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lactoferricin is a ***peptide*** derived from the cleavage of the amino-terminal region of ***lactoferrin*** by the proteolytic enzyme pepsin in the stomach. Many of the physiol. activities of ***lactoferrin*** are in fact contained in this 25-residue ***peptide***. For example, lactoferricin is a much more potent antimicrobial agent than the intact protein. We have shown earlier that release of the ***peptide*** is accompanied by a large conformational change, which explains the increased potency. Many antimicrobial ***peptides*** act on bacterial membranes. Hence we have investigated the mechanism of binding of shortened versions of the ***peptide*** to membrane mimetic micelles and vesicles. Using NMR spectroscopy we have

detd. the structure of two membrane-bound linear 6- and 11-residue ***peptides*** , as well as a ***cyclized*** version of the 11-mer ***peptide*** . In addn. we have used fluorescence spectroscopy and calorimetry methods to study the binding of these ***peptides*** to vesicles of distinct compn. Several 15-residue ***analogs*** of the lactoferricin ***peptide*** with amino acid substitutions were also studied. Together these studies have shown that two Trp and several Arg residues are crucial for the antimicrobial activity of these ***peptides*** . Hence lactoferricin, appears to be part of a group of Trp/Arg-rich antimicrobial ***peptides*** , such as those found in white blood cells of bovine and porcine origin. Similar Trp/Arg-rich ***peptides*** have also been identified by combinatorial chem. methods. Their Arg residues allow them to bind preferentially to the neg. charged phospholipids in bacterial membranes, while the Trp residues play an important role as a membrane-interface "anchor". Binding to eukaryotic membranes is less efficient as these are primarily composed of zwitterionic phospholipids, which have no net charge. In contrast, cancer cells have more neg. charged phospholipids on the outer leaflet of their membranes, explaining perhaps how lactoferricin can act selectively on cancer cells. Our results, combined with the work from other groups, point towards a mechanism of action for lactoferricin and related shorter ***peptides*** , where its interaction with biol. membranes plays an important role.

L5 ANSWER 3 OF 9 MEDLINE DUPLICATE 1
 ACCESSION NUMBER: 2001374396 MEDLINE
 DOCUMENT NUMBER: 21324153 PubMed ID: 11431038
 TITLE: Lactoferrin and cyclic lactoferricin inhibit the entry of human cytomegalovirus into human fibroblasts.
 AUTHOR: Andersen J H; Osbakk S A; Vorland L H; Traavik T; Gutteberg T J
 CORPORATE SOURCE: Department of Microbiology, University Hospital of Tromso, N 9038 Tromso, Norway.. mlabjeh@rito.no
 SOURCE: ANTIVIRAL RESEARCH, (2001 Aug) 51 (2) 141-9. Journal code: 8109699. ISSN: 0166-3542.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200109
 ENTRY DATE: Entered STN: 20011001
 Last Updated on STN: 20011001
 Entered Medline: 20010927
 AB ***Lactoferrin*** is mainly produced by polymorphonuclear leukocytes and has been demonstrated in mammalian milk and external secretions. ***Lactoferrin*** is an iron-binding, multifunctional protein and may play an important role in immune regulation and in defense mechanisms against bacteria, fungi and viruses. Lactoferricin is a potent antimicrobial ***peptide*** generated from the N-terminal part of ***lactoferrin*** by pepsin cleavage. We demonstrate that ***lactoferrins*** from different species and its N-terminal ***peptide*** lactoferricin (particularly the ***cyclic*** form) inhibit expression of early and late antigens, as well as production of infectious viral progeny during human cytomegalovirus (HCMV) infection in vitro. Iron-saturated ***lactoferrin*** did not affect HCMV antigen expression. Heparin had the same effects as iron-depleted

lactoferrin . Yet, mixtures of ***lactoferrin*** and heparin did not inhibit HCMV multiplication i.e. ***lactoferrin*** and heparin seemed to mutually block each other's antiviral activities. HCMV-infected cells exposed to ***lactoferrin*** and ***cyclic*** lactoferricin contained less intracellular virus than unexposed cells. The antiviral activity of ***cyclic*** lactoferricin was more than seven-fold weaker than that of the maternal molecule. ***Lactoferrin*** and ***cyclic*** lactoferricin prevented HCMV entrance into the host cell.

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:161316 CAPLUS

DOCUMENT NUMBER: 132:208139

TITLE: Preparation of antimicrobial peptides

INVENTOR(S): Svendsen, John Sigurd; Rekdal, Oystein;

Sveinbjornsson, Baldur; Vorland, Lars

PATENT ASSIGNEE(S): Alpharma As, Norway; Gardner, Rebecca

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2000012542 | A2 | 20000309 | WO 1999-GB2851 | 19990831 |
| WO 2000012542 | A3 | 20000629 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2341037 | AA | 20000309 | CA 1999-2341037 | 19990831 |
| AU 9955268 | A1 | 20000321 | AU 1999-55268 | 19990831 |
| EP 1109827 | A2 | 20010627 | EP 1999-941774 | 19990831 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| WO 2001019852 | A2 | 20010322 | WO 2000-GB3378 | 20000831 |
| WO 2001019852 | A3 | 20020912 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1259536 | A2 | 20021127 | EP 2000-956720 | 20000831 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |

US 2003022821 A1 20030130 US 2001-798869 20010227
NO 2002000950 A 20020425 NO 2002-950 20020227
PRIORITY APPLN. INFO.: GB 1998-18938 A 19980828
WO 1999-GB2851 W 19990831
GB 2000-5702 A 20000309
WO 2000-GB3378 W 20000831

AB Cytotoxic modified ***lactoferrin*** ***peptides*** having 7 to 25 amino acids with three or more cationic residues and one or more extra bulky and lipophilic amino acids as compared to the native ***lactoferrin*** sequence, as well as their esters, amides, salts and ***cyclic*** derivs., were prepd. as antibacterial and antitumoral agents. Syntheses were carried by the solid-phase method. Antibacterial test data are tabulated for >200 ***peptides***.

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:382962 CAPLUS

DOCUMENT NUMBER: 133:148083

TITLE: Regulatory effect of bovine lactoferricin on the cell cycle in human monocytic THP-1 cells

AUTHOR(S): Yoo, Yung-Choon; Watanabe, Ryosuke; Shimazaki, Kei-Ichi; Paik, Tae Hyun; Azuma, Ichiro

CORPORATE SOURCE: Department of Microbiology, College of Medicine, Konyang University, Nonsan City, 320-711, S. Korea

SOURCE: International Congress Series (2000), 1195(Lactoferrin: Structure, Function and Applications), 163-171
CODEN: EXMDA4; ISSN: 0531-5131

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We investigated the effect of a bovine ***lactoferrin*** (LF-B)-derived ***peptide***, lactoferricin (Lfcin-B), on regulation of cell cycle during apoptosis induction in human monocytic THP-1 cells. Treatment with Lfcin-B, but not B-LF, induced cell death in THP-1 cells in a time-dependent manner, showing apparent hypodiploid forms of genomic DNA. Anal. of cell cycle progression by bromodeoxyuridine (BrdU) labeling method revealed that THP-1 cells exposed by Lfcin-B did not progress into S phase (G1 arrest). Furthermore, THP-1 cells synchronized at G1 phase, followed by Lfcin-B treatment, were not able to progress into S phase, and the cells displayed cell death time-dependent manner. Western blot, using various monoclonal antibodies specific to ***cyclin*** D2, ***cyclin*** E, ***cyclin***-dependent kinase 2 (CDK2) and CDK4, and regulatory mols. responsible for cell cycle progression of G1 phase into S phase, showed that G1 arrest induced by Lfcin-B was related to downregulation of expression of these cell cycle regulatory mols. Interestingly, the addn. of an antioxidant, N-acetylcystein (NAC), completely abrogated the effect of Lfcin-B to induce G1 arrest in THP-1 cells. These results suggested that Lfcin-B induces G1 arrest during apoptosis in THP-1 cells, and the regulation of cell cycle by Lfcin-B is controlled by reactive oxygen species (ROS) at a point up-stream of the apoptosis cascade.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 1999163939 MEDLINE

DOCUMENT NUMBER: 99163939 PubMed ID: 10066056
TITLE: Lactoferricin of bovine origin is more active than
lactoferricins of human, murine and caprine origin.
AUTHOR: Vorland L H; Ulvatne H; Andersen J; Haukland H; Rekdal O;
Svendsten J S; Gutteberg T J
CORPORATE SOURCE: Department of Medical Microbiology, University Hospital,
Tromsø, Norway.
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1998) 30 (5)
513-7.
Journal code: 0215333. ISSN: 0036-5548.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990511
Last Updated on STN: 19990511
Entered Medline: 19990427

AB The antimicrobial ***peptide*** lactoferricin is generated by gastric
pepsin cleavage of ***lactoferrin***. We have examined the
antimicrobial activity of lactoferricins derived from ***lactoferrin***
of human, murine, caprine and bovine origin with minimal inhibitory
concentration (MIC) and minimal bactericidal concentration (MBC) against
E. coli ATCC 25922 and S. aureus ATCC 25923. We found that lactoferricin
of bovine origin (Lf-cin B) was the most efficacious of the lactoferricins
tested. By comparing the linear and ***cyclic*** Lf-cin B we found the
cyclic ***peptide*** to be the most active. Lactoferricin B
was moderately active against E. coli ATCC 25922 and S. aureus ATCC 25923,
but had no activity against P. mirabilis or Y. enterocolitica. Lf-cin B
showed good activity against C. albicans, C. tropicalis and C. neoformans.

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 1996:117036 CAPLUS
DOCUMENT NUMBER: 124:261711
TITLE: On the "immunostimulative" and "immunosuppressive"
conformation of thymopentin analogs
AUTHOR(S): Siemion, I. Z.; Szewczuk, Z.; Kluczyk, A.; Slon, J.
J.; Wieczorek, Z.
CORPORATE SOURCE: Inst. Chem., Univ. Wroclaw, Wroclaw, 50-383, Pol.
SOURCE: Polish Journal of Chemistry (1995), 69(12), 1669-78
CODEN: PJCHDQ; ISSN: 0137-5083
PUBLISHER: Polish Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of structural ***analogs*** of ***lactoferrin***
immunosuppressive pentapeptide Arg-Lys-Pro-Val-Asp (I) were investigated
for their immunomodulatory activity. The series consisted of the
following compds.: Arg-Lys-Pro-Val-D-Asp, Arg-Lys-D-Pro-Val-Asp,
Cys(Acm)-Arg-Lys-Pro-Val-Asp-Cys(Acm), Cys(Acm)-Arg-Lys-D-Pro-Val-Asp-
Cys(Acm) and two ***cyclic*** ***peptides***, the disulfides of
H-Cys-Arg-Lys-Pro-Val-Asp-Cys-OH and H-Cys-Arg-Lys-D-Pro-Val-Asp-Cys-OH.
All of these compds. demonstrate immunosuppressive activity of diverse
range regarding humoral and cellular immune response. The conformation of
I from X-ray data (as the model "immunosuppressive" conformation) is
compared with the "immunostimulative" conformation proposed for
thymopentin. The tolerance of the bioactive conformation of I to the

configurational change on the central Pro residue was also investigated.

L5 ANSWER 8 OF 9 SCISEARCH COPYRIGHT 2003 ISI (R)

ACCESSION NUMBER: 91:329343 SCISEARCH

THE GENUINE ARTICLE: FP691

TITLE: HISTAMINE INHIBITS CELL SPREADING AND C3BI RECEPTOR
CLUSTERING AND DIMINISHES HYDROGEN-PEROXIDE PRODUCTION BY
ADHERENT HUMAN NEUTROPHILS

AUTHOR: FRANCIS J W (Reprint); TODD R F; BOXER L A; PETTY H R

CORPORATE SOURCE: WAYNE STATE UNIV, DEPT BIOL SCI, DETROIT, MI, 48202
(Reprint); UNIV MICHIGAN, SCH MED, DEPT PEDIAT, ANN ARBOR,
MI, 48109; UNIV MICHIGAN, SCH MED, DEPT INTERNAL MED, ANN
ARBOR, MI, 48109

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (1991) Vol. 147, No. 1,
pp. 128-137.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 77

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cell adherence plays a central role in many host defense mechanisms.

Human peripheral blood neutrophils possess cell surface receptors that contribute to cell adherence or detachment. Receptors specific for the C3bi cleavage fragment of the third component of complement (CR3) promote adhesion, whereas histamine receptors promote detachment. In the present study, we tested the ability of histamine to down-regulate the physiological effects of CR3 receptors. Histamine decreased the binding of Cr-51-labeled neutrophils to complement-coated surfaces (C3-coated surfaces) in a dose-dependent fashion. Scanning electron microscopic and optical microscopic observations of neutrophils on C3-coated surfaces revealed polarized or spherical cell morphologies in the absence or presence of histamine, respectively. Histamine inhibited the ability of CR3 to cluster on plasma membranes of neutrophils adherent to C3-coated surfaces as shown by fluorescence microscopy. In addition, histamine diminished but did not abolish the FMLP-stimulated increase in plasma membrane CR3 expression as measured by fluorometry. Histamine did not inhibit the release of marker proteins from specific or gelatinase containing granules by neutrophils in suspension. Histamine also diminished the FMLP-stimulated production of respiratory burst oxidants from cells in suspension or cells allowed to adhere to fibrinogen substrates. We suggest that histamine may modulate selective changes in neutrophil function by diminishing adherence and preventing changes in cell shape following cell activation.

L5 ANSWER 9 OF 9 MEDLINE

DUPLICATE 4

ACCESSION NUMBER: 90336734 MEDLINE

DOCUMENT NUMBER: 90336734 PubMed ID: 2165916

TITLE: Impaired receptor binding and decrease in isoelectric point
of lactoferrin after interaction with human monocytes.

AUTHOR: Birgens H S; Kristensen L O

CORPORATE SOURCE: Department of Medicine and Haematology C, Gentofte
Hospital, University of Copenhagen, Hellerup, Denmark.

SOURCE: EUROPEAN JOURNAL OF HAEMATOLOGY, (1990 Jul) 45 (1) 31-5.
Journal code: 8703985. ISSN: 0902-4441.

PUB. COUNTRY: Denmark

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199009

ENTRY DATE: Entered STN: 19901012

Last Updated on STN: 19970203

Entered Medline: 19900910

AB The iron-binding glycoprotein ***lactoferrin*** binds to specific receptors on human monocytes as an initial step implicated in monocytic iron deposition. In this study, the properties of ***lactoferrin*** were studied after its interaction with human monocytes. Rebinding of ***lactoferrin*** to its monocytic receptor was grossly impaired and a small decrease in isoelectric point from 8.9 to 8.8 was observed. In contrast, antigenic and iron-binding properties of ***lactoferrin*** were preserved, the molecular weight by SDS-polyacrylamide gel electrophoresis was unchanged and no low-molecular ***fragments*** were detected by gel-filtration. These findings indicate that ***lactoferrin*** molecules cannot operate in a ***cyclic*** manner to deposit iron. Furthermore, these results might contribute towards explaining the complex disappearance kinetics observed for ***lactoferrin*** in plasma.

=> d his

(FILE 'HOME' ENTERED AT 12:10:39 ON 26 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:11:04 ON 26 FEB 2003

L1 20298 S LACTOFERRIN
L2 1889 S (PEPTIDE OR FRAGMENT OR ANALOG) (P) L1
L3 0 S L2 (P) 21-30
L4 20 S L2 (P) CYCLI?
L5 9 DUPLICATE REMOVE L4 (11 DUPLICATES REMOVED)

=> s l2 (p) (acetyl原因? or amidat?)

L6 4 L2 (P) (ACETYLAT? OR AMIDAT?)

=> duplicate remove l6

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L6

L7 1 DUPLICATE REMOVE L6 (3 DUPLICATES REMOVED)

=> d l7 1 ibib abs

L7 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 81265471 MEDLINE
DOCUMENT NUMBER: 81265471 PubMed ID: 6267133
TITLE: Activation of human neutrophils with 1-O-
hexadecyl/octadecyl-2-acetyl-sn-glycerol-3-
phosphorylcholine (platelet activating factor).
AUTHOR: Shaw J O; Pinckard R N; Ferrigni K S; McManus L M; Hanahan
D J
CONTRACT NUMBER: HL-22555 (NHLBI)
HL-23578 (NHLBI)

SOURCE: JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 1250-5.

Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198110

ENTRY DATE: Entered STN: 19900316

Last Updated on STN: 19970203

Entered Medline: 19811029

AB 1-O-Hexadecyl/octadecyl-2-acetyl-sn-glycerol-3-phosphorylcholine (AGEPC), the ***acetylated*** alkyl phosphoglyceride known as platelet-activating factor, stimulated human neutrophil (PMN) exocytosis, migration, superoxide production and aggregation over a concentration range of 10^{-10} to 10^{-5} M. AGEPC-induced PMN exocytosis of azurophilic (myeloperoxidase and beta-glucuronidase) and specific (***lactoferrin*** and lysozyme) lysosomal granules was rapid ($T_{1/2} = 20$ sec), dependent on the presence of cytochalasin B, but was not associated with release of cytoplasmic LDH. As seen with the complement-derived ***peptide*** stimulus, C5a, AGEPC-initiated PMN enzyme release was dependent on temperature and cellular glycolysis but not on the presence of extracellular Ca^{++} . When analyzed by gradient analysis, PMN migration caused by AGEPC was primarily chemotactic in nature. An unusual feature for both enzyme secretion and migration was a decrease in response between 10^{-6} M and 10^{-5} M AGEPC. This decreased responsiveness could be explained by rapid PMN desensitization occurring at high AGEPC concentrations, limiting the overall cellular response. Rapid desensitization for exocytosis was demonstrated in PMN stimulated with AGEPC in the absence of cytochalasin B. When cytochalasin B was added subsequently and PMN challenged with AGEPC or C5a, stimulus-specific desensitization to AGEPC but not C5a-induced lysosomal enzyme release occurred. PMN desensitized to C5a responded normally to a subsequent AGEPC challenge. Stimulation of all the PMN functions examined was markedly attenuated with removal of the 2-acetyl group from AGEPC (lyso GEPC). These results suggest that AGEPC stimulates a wide variety of human PMN responses by a receptor-like mechanism, dependent on the short chain fatty acid ester in the 2-position of the alkyl phosphoglyceride.

=> s (medical product) or (food stuff) or (infant formula)

L8 14675 (MEDICAL PRODUCT) OR (FOOD STUFF) OR (INFANT FORMULA)

=> d his

(FILE 'HOME' ENTERED AT 12:10:39 ON 26 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:11:04 ON 26 FEB 2003

L1 20298 S LACTOFERRIN

L2 1889 S (PEPTIDE OR FRAGMENT OR ANALOG) (P) L1

L3 .0 S L2 (P) 21-30

L4 20 S L2 (P) CYCLI?

L5 9 DUPLICATE REMOVE L4 (11 DUPLICATES REMOVED)

L6 4 S L2 (P) (ACETYLAT? OR AMIDAT?)

L7 1 DUPLICATE REMOVE L6 (3 DUPLICATES REMOVED)

L8 14675 S (MEDICAL PRODUCT) OR (FOOD STUFF) OR (INFANT FORMULA)

=> s l8 (p) l2
L9 18 L8 (P) L2

=> duplicate remove l9
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L9
L10 6 DUPLICATE REMOVE L9 (12 DUPLICATES REMOVED)

=> d l10 1-6 ibib abs

L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:234465 CAPLUS
TITLE: Bovine lactoferrin and lactoferricin derived from
milk: production and applications
AUTHOR(S): Tomita, M.; Wakabayashi, H.; Yamauchi, K.; Teraguchi,
S.; Hayasawa, H.
CORPORATE SOURCE: Nutritional Science Laboratory, Morinaga Milk Industry
Co. Ltd., Kanagawa, 228-8583, Japan
SOURCE: Biochemistry and Cell Biology (2002), 80(1), 148
CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bovine ***lactoferrin*** (bLF) is produced on an industrial scale (approx. 20-30 tons annually worldwide) from cheese whey or skim milk. The safety of bLF has been confirmed from the results of a reverse mutation test using bacteria, a 13-wk oral repeated dose toxicity study in rats (no adverse effects at 2000 mg/kg/day), and clin. studies. In order to apply active bLF to various products, pasteurization of LF was achieved by heat treatment at an acidic pH. Subsequently, bLF has been used in a large variety of products since it was first added to ***infant*** ***formula*** in 1986. A pepsin hydrolyzate of bLF is also used in ***infant*** ***formula***. The hydrolyzate contains a potent antimicrobial ***peptide*** named Lactoferricin B (LFcin B) that is derived from the N-terminal region of bLF by pepsin digestion. Semi-large scale purifn. of LFcin B can be performed by hydrophobic interaction chromatog. LFcin B also exhibits several biol. actions other than antimicrobial activity and appears to be a domain that contains the integrated functions of Lf. Recent reports have demonstrated that orally administered bLF or LFcin B exerts a host-protective effect in various animal models and in humans, including patients with tinea pedis and chronic hepatitis C. The results of these studies strongly suggest that the effects of oral bLF are mediated by modulation of the immune system. Further elucidation of the clin. efficacy and mechanism of action of bLF will increase the value of bLF products.

L10 ANSWER 2 OF 6 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002176192 MEDLINE
DOCUMENT NUMBER: 21905317 PubMed ID: 11908633
TITLE: Bovine lactoferrin and lactoferricin derived from milk:
production and applications.
AUTHOR: Tomita M; Wakabayashi H; Yamauchi K; Teraguchi S; Hayasawa
H
CORPORATE SOURCE: Nutritional Science Laboratory, Morinaga Milk Industry Co.,

Ltd., Zama, Kanagawa, Japan.
SOURCE: BIOCHEMISTRY AND CELL BIOLOGY, (2002) 80 (1) 109-12. Ref:
28
Journal code: 8606068. ISSN: 0829-8211.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020324
Last Updated on STN: 20021012
Entered Medline: 20021011

AB Bovine ***lactoferrin*** is produced on an industrial scale from cheese whey or skim milk. The safety of purified ***lactoferrin*** has been confirmed from the results of a reverse mutation test using bacteria, a 13-week oral repeated-dose toxicity study in rats, and clinical studies. In order to apply active ***lactoferrin*** to various products, a process for its pasteurization was developed. Subsequently, ***lactoferrin*** has been used in a wide variety of products since it was first added to ***infant*** ***formula*** in 1986. A pepsin hydrolysate of ***lactoferrin*** is also used in ***infant*** ***formula***. This hydrolysate contains a potent antimicrobial ***peptide*** named lactoferricin that is derived from the ***lactoferrin*** molecule by pepsin digestion. Semilarge-scale purification of lactoferricin can be performed by hydrophobic interaction chromatography. Lactoferricin also exhibits several biological actions and appears to be the functional domain of ***lactoferrin***. Recent studies have demonstrated that oral administration of ***lactoferrin*** or lactoferricin exerts a host-protective effect in various animals and in humans. The results of these studies strongly suggest that the effects of oral ***lactoferrin*** are mediated by modulation of the immune system. Further elucidation of the clinical efficacy and mechanism of action of ***lactoferrin*** will increase the value of ***lactoferrin***-containing products.

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:34905 CAPLUS

DOCUMENT NUMBER: 132:113080

TITLE: Peptides based on the sequence of human lactoferrin
and their use in prevention and treatment of
infections, inflammations, and tumors

INVENTOR(S): Hanson, Lars A.; Mattsby-Baltzer, Inger; Baltzer,
Lars; Dolphin, Gunnar T.

PATENT ASSIGNEE(S): A+ Science Invest AB, Swed.

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2000001730 | A1 | 20000113 | WO 1999-SE1230 | 19990706 |

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU,
 CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
 LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
 SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2333306 AA 20000113 CA 1999-2333306 19990706
 AU 9950760 A1 20000124 AU 1999-50760 19990706
 AU 752640 B2 20020926
 EP 1095061 A1 20010502 EP 1999-935241 19990706
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 JP 2002519438 T2 20020702 JP 2000-558131 19990706
 PRIORITY APPLN. INFO.: SE 1998-2441 A 19980706
 SE 1998-2562 A 19980717
 SE 1998-4614 A 19981229
 WO 1999-SE1230 W 19990706
 OTHER SOURCE(S): MARPAT 132:113080
 AB The invention relates to new ***peptides*** formed of at least seven
 subsequent amino acids of the amino acids in position 12-40, counted from
 the N-terminal end, in the sequence constituting human ***lactoferrin***
 , and preferably modifications thereof. The invention also relates to
 medicinal products comprising such ***peptides*** , esp. intended for
 treatment and prevention of infections, inflammations and tumors.
 Furthermore, the invention relates to ***food*** ***stuff*** , e.g.
 infant ***formula*** food, comprising the above mentioned
 peptides .
 REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
 L10 ANSWER 4 OF 6 MEDLINE DUPLICATE 2
 ACCESSION NUMBER: 1999117119 MEDLINE
 DOCUMENT NUMBER: 99117119 PubMed ID: 9920391
 TITLE: Direct evidence of the generation in human stomach of an
 antimicrobial peptide domain (lactoferricin) from ingested
 lactoferrin.
 AUTHOR: Kuwata H; Yip T T; Tomita M; Hutchens T W
 CORPORATE SOURCE: Department of Food Science and Technology, University of
 California, Davis 95616, USA.. hidi@msn.com
 SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Dec 8) 1429 (1)
 129-41.
 Journal code: 0217513. ISSN: 0006-3002.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199902
 ENTRY DATE: Entered STN: 19990301
 Last Updated on STN: 19990301
 Entered Medline: 19990216
 AB The ability to define specific alterations in the structure and function
 of proteins as they are introduced and processed in vivo remains an
 important goal. We have evaluated the generation, in vivo, of an

antimicrobial ***peptide*** (lactoferricin) derived from ingested bovine ***lactoferrin*** by surface-enhanced laser desorption/ionization (SELDI). SELDI was used in the affinity mass spectrometry operational mode to detect and quantify lactoferricin directly from unfractionated gastric contents using a chemically defined ligand with a terminal n-butyl group as the lactoferricin affinity capture device. By this method, we were able to detect and quantify lactoferricin directly upon examination of unfractionated gastric contents recovered from an adult subject 10 min after ingestion of bovine ***lactoferrin*** (200 ml of 10 mg/ml (1.2×10^{-4}) mol/l) solution). Lactoferricin produced in vivo was directly captured by a surface-enhanced affinity capture (SEAC) device composed of molecules with a terminal n-butyl group and analyzed by laser desorption/ionization time-of-flight mass spectrometry. The recovery of standard lactoferricin or ***lactoferrin*** added to an aliquot of the gastric contents was determined to be nearly 100%, confirming the efficiency of this method. The amount of lactoferricin detected in the gastric contents was 16.9 ± 2.7 microg/ml ($5.4 \pm 0.8 \times 10^{-6}$) mol/l). However, a large proportion of ingested ***lactoferrin*** was found to be incompletely hydrolyzed. ***Lactoferrin***

fragments containing the lactoferricin region were analyzed by in situ pepsin hydrolysis after being captured on the SEAC device. Partially degraded ***lactoferrin*** ***fragments*** containing the lactoferricin region, including ***fragments*** corresponding to positions 17-43, 17-44, 12-44, 9-58 and 16-79 of the bovine

lactoferrin sequence, were found to be present at concentrations as high as $5.7 \pm 0.7 \times 10^{-5}$ mol/l. These results suggest that significant amounts of bovine lactoferricin would be produced in the human stomach following ingestion of food, such as ***infant***

formula, supplemented with bovine ***lactoferrin***. We propose that physiologically functional quantities of human lactoferricin could be generated in the stomach of breast-fed infants, and possibly, in the case of adults, from ***lactoferrin*** secreted into saliva.

L10 ANSWER 5 OF 6 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998454624 MEDLINE
DOCUMENT NUMBER: 98454624 PubMed ID: 9781339
TITLE: Direct detection and quantitative determination of bovine lactoferricin and lactoferrin fragments in human gastric contents by affinity mass spectrometry.
AUTHOR: Kuwata H; Yip T T; Yip C L; Tomita M; Hutchens T W
CORPORATE SOURCE: Department of Food Science and Technology, University of California, Davis, USA.
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 443 23-32.
Journal code: 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981209
AB Lactoferricin (Lfcin) is a bioactive ***fragment*** of ***lactoferrin*** derived from the bactericidal and putative lymphocyte receptor binding domain(s) located within the N-lobe of

lactoferrin . Although known to be liberated from at least three species of ***lactoferrin*** , conditions leading to Lfcin generation in vivo and factors affecting its distribution are still not known. Recently, we have developed a method of surface-enhanced laser desorption/ionization (SELDI) affinity mass spectrometry using n-butyl terminal groups for surface-enhanced affinity capture (SEAC) to quantify not only Lfcin generated in vivo but also other ***lactoferrin*** ***fragments*** . Unlike previous efforts to detect ***lactoferrin*** and Lfcin with specific antibodies, the SELDI affinity assay distinguished ***lactoferrin*** , ***lactoferrin*** ***fragments*** , Lfcin and unrelated ***peptides*** without their interference with each other. To evaluate Lfcin generation in vivo, the experimental design involved feeding 200 mL of 10 mg/mL (1.22×10^{-4}) mol/L bovine ***lactoferrin*** to an adult. Gastric contents were recovered 10 min after ingestion. Lfcin produced in vivo was directly captured by the SEAC device. The amount of Lfcin in the gastric contents was 16.91 ± 2.65 micrograms/mL ($5.350 \pm 0.838 \times 10^{-6}$) mol/L. However, a large proportion of the ingested ***lactoferrin*** was not completely digested. ***Lactoferrin*** ***fragments*** containing the Lfcin region were analyzed by in situ hydrolysis with pepsin after being captured by the SEAC device. As much as $5.740 \pm 0.702 \times 10^{-5}$ mol/L of the partially degraded ***lactoferrin*** ***fragments*** were found to contain the Lfcin region, including ***peptide*** domains 17-43, 17-44, 12-44, 9-58, and 16-76 of bovine ***lactoferrin*** . These results show that bovine Lfcin can be produced in the human stomach after ingestion of an ***infant*** ***formula*** supplemented with bovine ***lactoferrin*** . It is now important to determine whether Lfcin is generated in the intestinal tract of formula-fed and breast-fed infants, and geriatric patients consuming foods enriched with ***lactoferrin*** .

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4

ACCESSION NUMBER: 1996:249818 CAPLUS

DOCUMENT NUMBER: 124:284135

TITLE: Antibacterial activity of lactoferricin, lysozyme and EDTA against Salmonella enteritidis

AUTHOR(S): Facon, Michel J.; Skura, Brent J.

CORPORATE SOURCE: Department of Food Science, University of British Columbia, Vancouver, BC, V6T 1Z4, Can.

SOURCE: International Dairy Journal (1996), 6(3), 303-13
CODEN: IDAJE6; ISSN: 0958-6946

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antibacterial activity of a pepsin digest of bovine

lactoferrin , contg. the ***peptide*** lactoferricin B, against Salmonella enteritidis was studied under various conditions. The digest had greater antibacterial activity than ***lactoferrin*** in 1% peptone, was bactericidal and also increased the permeability of the outer membrane of the bacteria as demonstrated by plating on bile salts agar. The antibacterial activity was inhibited in richer media, such as tryptic soy broth or milk-based or soy-based ***infant*** ***formula*** . Addn. of lysozyme or EDTA or both to the ***lactoferrin*** digest resulted in increased antibacterial activity of the mixt. Lysozyme or EDTA alone had little or no activity against S. enteritidis. The increase in antibacterial activity obtained with the addn. of lysozyme and EDTA to

the ***lactoferrin*** digest was not sufficient to overcome inhibition by components of the richer media.

=> d his

(FILE 'HOME' ENTERED AT 12:10:39 ON 26 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:11:04 ON 26 FEB 2003

L1 20298 S LACTOFERRIN
L2 1889 S (PEPTIDE OR FRAGMENT OR ANALOG) (P) L1
L3 0 S L2 (P) 21-30
L4 20 S L2 (P) CYCLI?
L5 9 DUPLICATE REMOVE L4 (11 DUPLICATES REMOVED)
L6 4 S L2 (P) (ACETYLAT? OR AMIDAT?)
L7 1 DUPLICATE REMOVE L6 (3 DUPLICATES REMOVED)
L8 14675 S (MEDICAL PRODUCT) OR (FOOD STUFF) OR (INFANT FORMULA)
L9 18 S L8 (P) L2
L10 6 DUPLICATE REMOVE L9 (12 DUPLICATES REMOVED)

=> s infection or inflammation or (urinary tract infection) or colitis or (CANDIDA OR INFECTION)
4 FILES SEARCHED...

L11 3360694 INFECTION OR INFLAMMATION OR (URINARY TRACT INFECTION) OR COLITIS OR (CANDIDA OR INFECTION)

=> s l2 (p) l11

L12 282 L2 (P) L11

=> s l12 and py<1999

3 FILES SEARCHED...

5 FILES SEARCHED...

L13 117 L12 AND PY<1999

=> duplicate remove l13

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L13

L14 49 DUPLICATE REMOVE L13 (68 DUPLICATES REMOVED)

=> s l14 (p) treat?

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L75 (P) TREAT?'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L77 (P) TREAT?'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L79 (P) TREAT?'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L81 (P) TREAT?'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L83 (P) TREAT?'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L85 (P) TREAT?'

L15 6 L14 (P) TREAT?

=> d l15 1-6 ibib abs

L15 ANSWER 1 OF 6 MEDLINE

ACCESSION NUMBER: 97079090 MEDLINE

DOCUMENT NUMBER: 97079090 PubMed ID: 8920822

TITLE: Lactoferrin-mediated protection of the host from murine
cytomegalovirus infection by a T-cell-dependent
augmentation of natural killer cell activity.

AUTHOR: Shimizu K; Matsuzawa H; Okada K; Tazume S; Dosako S;
Kawasaki Y; Hashimoto K; Koga Y

CORPORATE SOURCE: Department of Infectious Disease, Tokai University School
of Medicine, Kanagawa, Japan.

SOURCE: ARCHIVES OF VIROLOGY, *(1996)* 141 (10) 1875-89.
Journal code: 7506870. ISSN: 0304-8608.

PUB. COUNTRY: Austria

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199612

ENTRY DATE: Entered STN: 19970128

Last Updated on STN: 19970128

Entered Medline: 19961226

AB The administration of bovine *(lactoferrin)* (LF) with 1 mg/g body
weight before the murine cytomegalovirus (MCMV) *(infection)*
completely protected the BALB/c mice from death due to the
(infection). In these LF- *(treated)* mice, a significant
increase in the activity was found in the NK cells but not in the
cytolytic T lymphocytes which recognized an MCMV-derived *(peptide)*
. Moreover, the elimination of the NK cell activity by an injection with
anti-asialo GM1 antibody abrogated such augmented resistance, thus
supporting the hypothesis that the LF-mediated antiviral effect in vivo is
performed through the augmentation of NK cell activity. No such
LF-mediated antiviral effect in vivo with the increased NK cell activity
was found in athymic nude mice, whereas it was restored completely by the
transfer of splenic T cells from LF- *(treated)* donors. These
findings therefore suggest that T lymphocytes induce both the augmentation
of NK cell activity and the resultant antiviral effect in the LF-
(treated) hosts.

L15 ANSWER 2 OF 6 MEDLINE

ACCESSION NUMBER: 90122143 MEDLINE

DOCUMENT NUMBER: 90122143 PubMed ID: 2482056

TITLE: Enhanced plasma and intracellular levels of main
granulocyte components in diabetics on dialysis.

AUTHOR: Horl W H; Schaefer R M; Wanner C; Bahlmann J; Reitingner J;
Schollmeyer P; Heidland A

CORPORATE SOURCE: Department of Medicine, University of Freiburg, FRG.

SOURCE: BLOOD PURIFICATION, *(1989)* 7 (6) 314-23.
Journal code: 8402040. ISSN: 0253-5068.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199003

ENTRY DATE: Entered STN: 19900328

Last Updated on STN: 20000303

Entered Medline: 19900314

AB Intracellular and plasma levels of main granulocyte components (elastase, ***lactoferrin***) were investigated in 25 diabetic and 27 nondiabetic patients undergoing regular hemodialysis ***treatment*** (RDT) as well as in 14 diabetic and 11 nondiabetic patients undergoing continuous ambulatory peritoneal dialysis (CAPD). Diabetic patients on dialysis released more intragranular enzymes from neutrophils than their nondiabetic counterparts. Intracellular concentrations of granulocyte elastase and ***lactoferrin*** were only slightly higher in uremic diabetics than in uremic nondiabetics. However, both diabetic and nondiabetic hemodialysis patients displayed significantly lower cellular elastase and ***lactoferrin*** levels than healthy subjects. In addition, the diabetic dialysis patients had more protein catabolic ***fragments*** in the plasma as determined by trichloroacetic acid solubility. These observations were cited to support the hypothesis that not only is the hemodialysis procedure itself (with exposure to membranes) catabolic, but the diabetics are in double jeopardy. Thus, neutrophil abnormalities in diabetics on dialysis might affect the plasmatic proteinase inhibitor system and contribute to enhanced plasma protein degradation as well as to enhanced susceptibility to ***infections*** .

L15 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:91535 CAPLUS

DOCUMENT NUMBER: 134:142796

TITLE: Lactoferrin receptor genes of Moraxella catarrhalis

INVENTOR(S): Loosmore, Sheena M.; Du, Run-Pan; Wang, Quijun; Yang, Yan-Ping; Klein, Michel H.

PATENT ASSIGNEE(S): Connaught Laboratories Limited, Can.

SOURCE: U.S., 219 pp., Cont.-in-part of U.S. 5,977,337.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|--------------|
| US 6184371 | B1 | 20010206 | US 1998-74658 | 19980508 |
| US 5977337 | A | 19991102 | US 1997-867941 | 19970603 |
| WO 9855606 | A2 | 19981210 | WO 1998-CA544 | 19980602 <-- |
| WO 9855606 | A3 | 19990304 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9877534 | A1 | 19981221 | AU 1998-77534 | 19980602 <-- |
| AU 739129 | B2 | 20011004 | | |
| EP 1000144 | A2 | 20000517 | EP 1998-925352 | 19980602 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2001502925 | T2 | 20010306 | JP 1999-501181 | 19980602 |
| BR 9809914 | A | 20010918 | BR 1998-9914 | 19980602 |
| MX 9911210 | A | 20000630 | MX 1999-11210 | 19991203 |

PRIORITY APPLN. INFO.: US 1997-867941 A2 19970603
US 1998-74658 A 19980508
WO 1998-CA544 W 19980602

AB Purified and isolated nucleic acid mols. are provided which encode
lactoferrin receptor proteins of Moraxella, such as M.
catarrhalis, or a ***fragment*** or an ***analog*** of the
lactoferrin receptor protein. The nucleic acid sequence may be
used to produce recombinant ***lactoferrin*** receptor proteins Lbp1,
Lbp2, and ORF3 of the strain of Moraxella free of other proteins for
purposes of diagnostics and medical ***treatment***. Furthermore, the
nucleic acid mol. may be used in the diagnosis of ***infection***.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:806770 CAPLUS

DOCUMENT NUMBER: 130:63605

TITLE: Cloning and expression of lactoferrin receptor genes
of Moraxella catarrhalis and their clinical use

INVENTOR(S): Loosmore, Sheena M.; Du, Run-pan; Wang, Quijun; Yang,
Yan-ping; Klein, Michel H.

PATENT ASSIGNEE(S): Connaught Laboratories Ltd., Can.

SOURCE: PCT Int. Appl., 202 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|--------------|
| WO 9855606 | A2 | 19981210 | WO 1998-CA544 | 19980602 <-- |
| WO 9855606 | A3 | 19990304 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5977337 | A | 19991102 | US 1997-867941 | 19970603 |
| US 6184371 | B1 | 20010206 | US 1998-74658 | 19980508 |
| AU 9877534 | A1 | 19981221 | AU 1998-77534 | 19980602 <-- |
| AU 739129 | B2 | 20011004 | | |
| EP 1000144 | A2 | 20000517 | EP 1998-925352 | 19980602 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2001502925 | T2 | 20010306 | JP 1999-501181 | 19980602 |
| BR 9809914 | A | 20010918 | BR 1998-9914 | 19980602 |
| MX 9911210 | A | 20000630 | MX 1999-11210 | 19991203 |

PRIORITY APPLN. INFO.: US 1997-867941 A 19970603
US 1998-74658 A 19980508
WO 1998-CA544 W 19980602

AB The genes encoding ***lactoferrin*** receptor such as
lactoferrin binding protein (lbp) are isolated from Moraxella

catarrhalis strains 4223, Q8, and VH19 for developing diagnostic and therapeutic agents. A genomic DNA ***fragment*** of putative lfr locus from M. catarrhalis strains 4223 and Q8 contain genes lbpB (encoding Lbp2 protein), lbpA (Lbp1 protein), and open reading from orf3 (ORF3 protein). The DNA sequence may be used to produce recombinant ***lactoferrin*** receptor proteins Lbp1, Lbp2 or ORF3 for diagnostics and medical ***treatment***. Furthermore, the DNA mol. may be used in the diagnosis of ***infection*** by Moraxella.

L15 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:746210 CAPLUS

DOCUMENT NUMBER: 126:14777

TITLE: Agents for binding to advanced glycosylation end-products, and methods of their use

INVENTOR(S): Li, Yong Ming; Vlassara, Helen; Cerami, Anthony

PATENT ASSIGNEE(S): Picower Institute for Medical Research, USA

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|--------------|
| WO 9631537 | A1 | 19961010 | WO 1996-US4755 | 19960405 <-- |
| W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2217572 | AA | 19961010 | CA 1996-2217572 | 19960405 <-- |
| AU 9653869 | A1 | 19961023 | AU 1996-53869 | 19960405 <-- |
| EP 827511 | A1 | 19980311 | EP 1996-910765 | 19960405 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI | | | | |
| JP 11504316 | T2 | 19990420 | JP 1996-529784 | 19960405 |
| PRIORITY APPLN. INFO.: US 1995-418642 A 19950405 | | | | |
| US 1995-819P P 19950627 | | | | |
| WO 1996-US4755 W 19960405 | | | | |

OTHER SOURCE(S): MARPAT 126:14777

AB The present invention is directed to diagnostic and therapeutic methods based on the unexpected discovery that certain antibacterial proteins, in particular lysozyme and ***lactoferrin***, bind to advanced glycosylation end-products (AGEs) with high affinity, and that this binding activity is substantially noncompetitive with binding of bacterial carbohydrates to the antibacterial proteins. Accordingly, the invention relates to methods for ***treating*** diseases and disorders assocd. with increased levels of AGEs, by administering a mol. having a hydrophilic loop domain, which domain in lysozyme and ***lactoferrin*** is assocd. with AGE-binding activity, and compns. comprising such a domain. The invention further relates to methods and compns. for partitioning AGEs away from a sample. The invention is also directed to methods for detg. a prognosis of AGE complications in a patient suffering from an AGE-assocd. disease or disorder by measuring the level of activity

of antibacterial proteins, such as lysozyme and ***lactoferrin***, in a biol. sample from a subject. Decreased levels of antibacterial protein bactericidal activity may be indicative of increased levels of AGEs, and a prognostic indicator of increased susceptibility to bacterial ***infection***. In a further aspect, the invention relates to detection of AGEs in a biol. sample. In specific embodiments, AGEs inhibit the bactericidal activity of lysozyme and ***lactoferrin***, and 17- or 18-amino acid hydrophilic loop ***peptides*** bracketed by cysteine (the first and last amino acids are cysteine that form a disulfide bond) bind to AGE-bovine serum albumin.

L15 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:106533 CAPLUS

DOCUMENT NUMBER: 124:156014

TITLE: Topical preparations containing antifungal peptides

INVENTOR(S): Shimamura, Seiichi; Takase, Mitsunori; Yamauchi, Koji; Wakabayashi, Hiroyuki

PATENT ASSIGNEE(S): Morinaga Milk Industry Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|--------------|
| JP 07309774 | A2 | 19951128 | JP 1994-126882 | 19940517 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1994-126882 | 19940517 |

AB Topical preps. contain ***lactoferrin***-related antifungal ***peptides*** (sequences given) or their pharmaceutically acceptable derivs. or salts. The ***peptides*** can be prep'd. by automated ***peptide*** synthesizer. An O/W-type cream contained e.g. Phe-Gln-Trp-Gln-Arg-Asn 10, Me p-hydroxybenzoate 0.1, Pr p-hydroxybenzoate 0.1, propylene glycol 12, white petrolatum 25, stearyl alc. 20, ethoxylated castor oil 4, glycerin monostearate 1, and purified water 27.8g. The preps. are effective in ***treating*** skin ***infections*** such as trichophytosis and showed min. side effects.

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(FILE 'HOME' ENTERED AT 12:10:39 ON 26 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:11:04 ON 26 FEB 2003

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L1 20298 S LACTOFERRIN
L2 1889 S (PEPTIDE OR FRAGMENT OR ANALOG) (P) L1
L3 0 S L2 (P) 21-30
L4 20 S L2 (P) CYCLI?
L5 9 DUPLICATE REMOVE L4 (11 DUPLICATES REMOVED)
L6 4 S L2 (P) (ACETYLAT? OR AMIDAT?)
L7 1 DUPLICATE REMOVE L6 (3 DUPLICATES REMOVED)
L8 14675 S (MEDICAL PRODUCT) OR (FOOD STUFF) OR (INFANT FORMULA)
L9 18 S L8 (P) L2
L10 6 DUPLICATE REMOVE L9 (12 DUPLICATES REMOVED)

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L11 3360694 S INFECTION OR INFLAMMATION OR (URINARY TRACT INFECTION) OR COL
 L12 282 S L2 (P) L11
 L13 117 S L12 AND PY<1999
 L14 49 DUPLICATE REMOVE L13 (68 DUPLICATES REMOVED)
 L15 6 S L14 (P) TREAT?

=> log y

| COST IN U.S. DOLLARS | ENTRY | SINCE FILE SESSION | TOTAL |
|----------------------|-------|-----------------------|-------|
| FULL ESTIMATED COST | | 91.26 | 91.47 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | ENTRY | SINCE FILE SESSION | TOTAL |
|--------------------------------------------|-------|-----------------------|-------|
| CA SUBSCRIBER PRICE | | -7.81 | -7.81 |

STN INTERNATIONAL LOGOFF AT 12:20:24 ON 26 FEB 2003